

I. AMENDMENT

Please amend the above-identified application as follows:

In the Specification

Please replace paragraph 7, beginning at page 5, with the following rewritten paragraph:

Another variant similar to the Crameri system is the “cysteine-coupled” display system described in WO 01/05950. The attachment and display of the exogenous polypeptide are mediated by the formation of disulfide bond between two cysteine residues, one of which is contained in the exogenous sequence, and the other is inserted in the outer-surface sequence. The one vector system described in WO 01/05950 is a phagemid vector carrying two separate promoter-controlled expression cassettes: one expresses the exogenous sequence, and the another expresses the coat protein pIII. The two-vector system described in WO 01/05950 contains a phagemid vector carrying an exogenous sequence, and a plasmid expressing the coat protein pIII. The two vectors are used to co-transfect E. Coli cells. Upon superinfection with the helper phages, M13KO7, the phagemid and/or the plasmid are packaged into the resulting phage particles. Although this system avoids the expression of a fusion comprising the exogenous protein linked to an outer-surface protein, the system again fails to minimize the toxicity of coat proteins to the host cells because of the constitutive expression of the coat protein pIII in either the one-vector or the two-vector system. Furthermore, the two-vector system described in WO 01/05950 inevitably produces phage particles with mispackaged vectors carrying the outer-surface sequences and not the exogenous gene upon infection of the helper phages. Mispackaging is a well-known problem associated with two-vector system. It has been shown that the pIII-supplementing plasmid vectors were mispackaged into helper phage particles (Rondot et al. (2000) *Nature Biotechnology* **19**: 75-78).

Please replace paragraph 10, beginning at page 6, with the following rewritten paragraph:

A principal aspect of the present invention is the design of systems that enable display of polypeptides not linked to any outer-surface sequences of a genetic package via peptide bonds. The experimental design provides an unprecedented flexibility for the presentation and/or selection of proteins with desired properties on a genetic package such as a phage particle. The technical advantages of the subject phage-display system are manifold. First, the system avoids all drawbacks associated with expression of the outer-surface proteins by the expression vectors. As mentioned above, the drawbacks include (1) high toxicity to the host cell as a result of constitutive expression of the outer-surface sequences; (2) resistance of host cells to the infection of helper phages that is required for the production of progeny phage particles; (3) limitation on the orientation of the proteins to be displayed because of the unidirectional display of N-terminal fusion product; and (4) instability of the fusion product due to recombination between the fusion outer-surface sequence and the wildtype outer-surface sequence which is typically provided by the helper vector. Second, the system eliminates the possibility of mispackaging plasmids carrying the outer-surface sequences and not the gene of interest; such plasmids are used in the two-vector system described in WO 01/05950. While avoiding these and other intrinsic shortcomings of the prior display systems, the subject system further provides the flexibility of presenting one copy (monovalent display) or multiple copies (multivalent display) of a polypeptide per genetic package. The subject systems are particularly useful for expressing and screening a vast diverse repertoire of polypeptides (i.e. antigen-binding units) based on their ability to bind molecules of particular interest. The polypeptides displayed by the subject systems are functional.

Please replace paragraph 205, beginning at page 74, with the following rewritten paragraph:

The KpnI site was introduced into the gene III leader sequence of KO7 helper phage vector by PCR- based site-directed mutagenesis. The KO7 genome was amplified by PCR using the following primers which contain KpnI sites: p3KN1: 5'-TTTAGTGGTA CCTTTCTATTCTCACTCCGCTG-3' (SEQ ID NO. 19) and p3KN2: 5'-TAGAAAGGTACCACTAAAG GAATTGCGAATAA-3' (SEQ ID NO. 20). These primers share partial sequence homology to gene III leader sequence.

Please replace paragraph 216, beginning at page 79, with the following rewritten paragraph:

In the subject adapter-directed display system, the exogenous polypeptide of interest is expressed as a fusion with an adapter (designated adapter 1) which interacts with a paring adapter (designated “adaptor2”) that is fused in-frame with an outer-surface protein. The pairwise interaction between the two adapters facilitates display of the exogenous polypeptide. The phagemid vector pABMX14 is one of the expression vectors expressing an exogenous polypeptide fused in-frame with adapter 1. The vector pABMX14 (Figures 9A and 9B) was derived from pBluescript SK(+). A unique AgeI restriction site was introduced immediately after the lac promoter by PCR-based site-directed mutagenesis with a set of primers (pBS-Ska: 5'-GGAATTGTGAGCGGAT AACAATTTACCGGTCACACAGGAAACAGCTATGA-CCATG-3' (SEQ ID NO. 21) and pBS-SKb: 5'-CATGGTCATAGCTGTTTCCTGTGTGACCGGTAAATT-GTTATCCGCTCACAAT-T-CC-3' (SEQ ID NO. 22)), and the XhoI and KpnI sites were deleted by cutting and blunt-end ligation. The synthetic DNA fragment flanked by AgeI at 5' and Sall sites at 3', containing ribosome-binding sequence RBS, pelB leader, and coding sequences for the adapter derived from GABA_B receptor 1 (GR1, as adaptor1) and HA-(His)₆-tag (referred to as DH-tag), was cloned into the engineered pBluescript SK(+). The lac Z promoter drives the expression of GR1 fusion and thus permits production of soluble exogenous polypeptide expressed with a bacterial cell.

In the Drawings:

Replacement Figure 3B identifies SEQ ID NOS. 1, 2, and 3.

Replacement Figure 5B identifies SEQ ID NOS. 4 and 5.

Replacement Figure 5C identifies SEQ ID NO. 6

Replacement Figure 9B identifies SEQ ID NO. 7.

Replacement Figure 13B identifies SEQ ID NOS. 8, 9, and 25.

Replacement Figure 15B identifies SEQ ID NO. 10.

Replacement Figure 19B identifies SEQ ID NOS. 11 and 12.

Replacement Figure 22B identifies SEQ ID NOS. 13, 14, and 26.

Replacement Figure 23 identifies SEQ ID NOS. 15, 16, 17 and 18.

Replacement Figure 25B identifies SEQ ID NO. 23.

Replacement Figure 26B identifies SEQ ID NO. 24.